

Original Research Article**Histopathological pattern of pediatric malignant tumors and survival rate at Kilimanjaro Christian Medical Centre, Tanzania from 2013 to 2015****ABSTRACT**

Background: Childhood malignant tumor is one among diseases that cause deaths to children below 14 years. Although it is the second most common cause of death in children in developed countries, its magnitude in Africa is not well known.

Aim: To determine the proportion of pediatric malignant tumors and the immediate outcome among children attending Kilimanjaro Christian Medical Centre in Tanzania.

Study design: Retrospective – hospital based study.

Place and Duration: Kilimanjaro Christian Medical Centre, Pathology department 3 years.

Methodology: Microscopic slides from January 2013 to December 2015 were retrieved from archives and evaluated at a magnification of 40x, 100x and 200x for histological features, diagnosis and disease grading. The findings were confirmed by the pediatric pathologist and concluded on the diagnoses and the grade. The tumors were graded into well differentiated and undifferentiated. Parents/guardians were contacted through phone calls to establish progress of their children to assess the six months survival rate.

Result: Among 84 studied patient slides, 43 (51.2%) were from males with the median (IQR) age of 4.5 (2.3-9.3) years. Children under five years of age were 50 (59.5%). Retinoblastoma was the most common malignant tumor accounting for 21 (25%) followed by Squamous cell carcinoma and Sarcoma with 13 (15.5%), respectively. Among 75 children other than patients with leukemia, 42 (56.0%) had well differentiated malignant tumors while 33 (44.0%)

undifferentiated. Forty-one (97.6%) of the patients with well-differentiated malignant tumors survived within six months from the date the specimen was taken. The overall six-month survival rate was 84.5%. Thirteen patients (15.5%) died during six months period from sample collection.

Conclusion: Retinoblastoma was the most common malignant tumor affecting children <14 years in northern Tanzania. The overall six-month survival rate was high when early detection of childhood malignancies is practicable.

Keywords: Histopathological pattern, pediatric, malignant tumor, tumor differentiation.

1. INTRODUCTION

Pediatric malignant tumors are among the leading killers in children below 14 years in the developed world while in Africa, it is not even ranked among the top ten causes of death [1]. Histologically, childhood malignancies manifest in different types including Retinoblastoma, Squamous cell carcinoma, Nephroblastoma, Leukemia, and Sarcoma. Inheritances of genetic susceptibility or spontaneous mutations have shown greater association with causes of cancers in children, because of the rapid cell proliferation that occurs at young ages [2]. However, the genetic basis for the most common types of childhood cancers has not been established except for retinoblastoma and Wilm's tumors [2].

The prevalence of pediatric malignancies varies between developed and developing countries. In Europe, Latin America and the USA, Leukemia has been reported as the leading malignant tumor [3-5] while in Africa, Lymphomas and Leukemia are the most leading malignant tumors in children [6]. In Tanzania-a study at the Ocean Road Cancer Institution has indicated that retinoblastoma is the most leading malignant tumor among pediatric malignancies [7].

Different types of pediatric malignancies have different survival rates and the rate differ between developed and developing countries. In developed countries the survival rate is higher (> 75%) [8] than in developing countries (<55%) [9]. This may be associated with availability of different and diagnostic methods and treatment.

Generally, little is known about the types of malignant tumors in children among children attending a tertiary hospital in northern Tanzania, therefore there is limitation in management and this can increase malignant tumors related morbidity/mortality in children. This study was carried out to determine the proportion and survival rate of pediatric malignant tumors at Kilimanjaro Christian Medical Centre in northern Tanzania between 2013 and 2015. Findings from this study will assist in the development of appropriate management protocol for tumor types.

2. METHODOLOGY

2.1 Study site

The study was conducted at Kilimanjaro Christian Medical Center; a referral, consultant, research and teaching hospital located in Moshi in northern Tanzania with a bed capacity of over 650. It provides medical services to a population of approximately 15.7 million people from Tanga, Kilimanjaro, Arusha and Manyara Regions. It processes and examines approximately 2,953 histology/cytology specimens per year for both adults and children.

2.2 Data collection

This was a retrospective hospital – based study. Structured data collection form was used to collect information. All children with malignancy aged 3 months to 14 years diagnosed by means of histology/cytology examination were recruited in the study. Microscopic slides, stained with Haematoxylin and Eosin were retrieved from archives and evaluated at a magnification of 40x, 100x and 200x, for histological features to diagnose and grade the disease. The tumors were graded into well-differentiated and undifferentiated tumors. Pediatric pathologist who was on site reviewed and confirmed the histological presentation and differentiation and together we concluded on the diagnosis and grade of the tumor. Identified cases were contacted through their parents or guardians to establish their progress. Patients who had complete data were included in the study.

2.3 Data analysis

Data were analysed using SPSS version 21.0. Descriptive statistics were used to summarize numerical data. The association between variables was analyzed using Chi-square test for categorical data. Odds of

events was tested using Odds Ratio (OR) at 95% Confidence Interval (CI). Tests were conducted at 5% level of significance.

3. RESULTS

A total of 101 patients were recruited in the study, of whom 17 (16.8%) were excluded in the study due to incomplete data. Out of 84 patients with malignancy 43 (51.2%) were males with the median (IQR) age of 4.5 (2.3-9.3) years (range= 0.25 - 14 years). Children under five years of age were 50 (59.5%). Among 84 patients, 34 (40.5%) were from Kilimanjaro and 31 (36.9%) were from Tanga and Arusha regions. Others were from Manyara, Singida, Shinyanga, Mwanza, Dodoma, Rukwa, Kigoma and Kenya (Table 1).

Table 1: Demographic characteristics (N=84)

Variable	No. (%)
Sex:	
Male	43 (51.2)
Female	41 (48.8)
Age (years):	
Median (IQR)	4.5 (2.3-9.3)
Under 5	50 (59.5)
5 - less than 10	16 (19.0)
10 – 14	18 (21.4)
Region:	
Kilimanjaro	34 (40.5)
Arusha	23 (27.4)
Tanga	8 (9.5)
Other	19 (22.6)

The most common clinical presentation was swelling (63.1%) followed by pain (10.7%) in the affected region or organ (Figure 2).

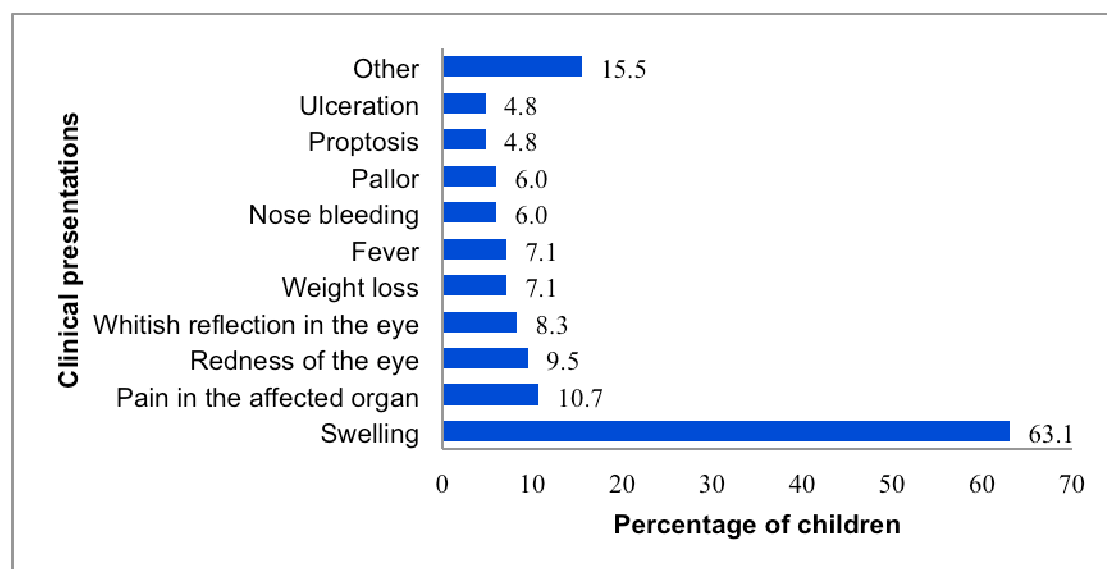


Figure 2: Distribution of clinical presentations (N=84)

The most commonly affected organ was the eye with 26 (31.0%) followed by skin with 19 (22.6%), (Figure 3).

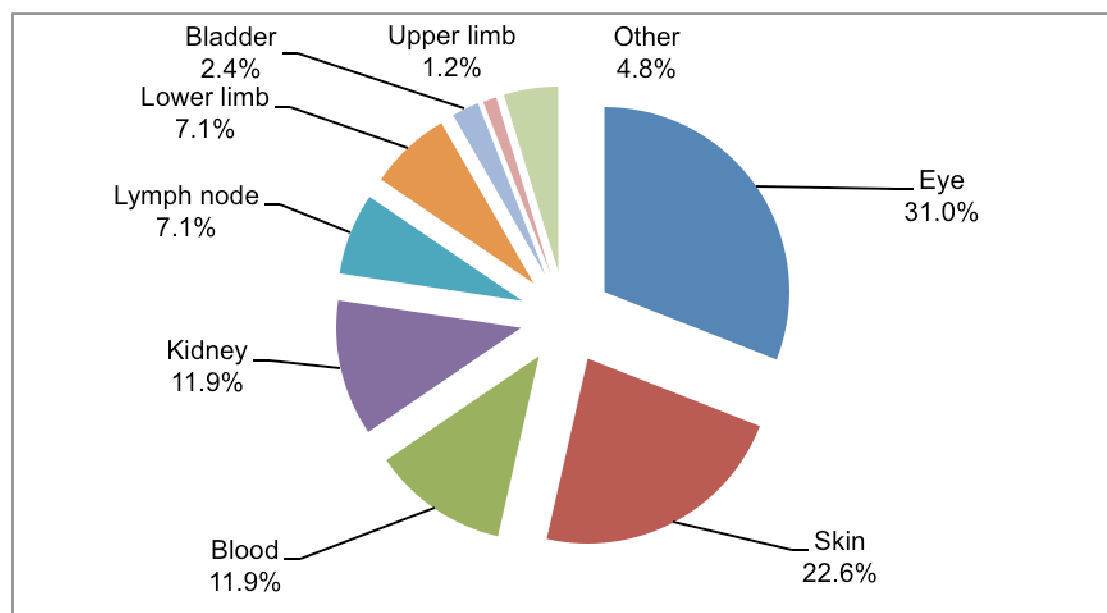


Figure 3: Organs affected (N=84)

The most common malignant tumors were retinoblastoma 21 (25.0%), Squamous cell carcinoma 13 (15.5%) and sarcoma 13 (15.5%). Sarcoma included Rhabdomyosarcoma 4 (4.8%), Kaposi's sarcoma 2 (2.4%), spindle cell sarcoma 3 (3.5%) and osteosarcoma 4 (4.8%). The remaining 8 (9.5%) included basal cell carcinoma, urothelial carcinoma, melanoma and adenocarcinoma (Figure 4).

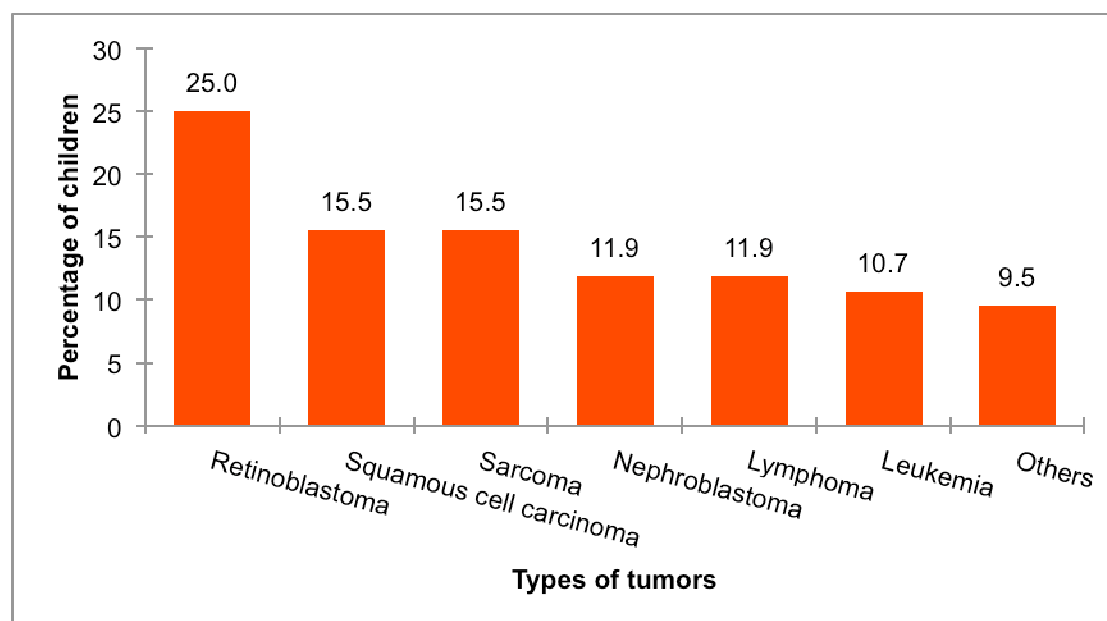


Figure 4: Distribution by Histopathological Diagnosis of malignant tumors (N=84)

Among 75 children with tumor differentiation, 42 (56.0%) had well differentiated malignant tumors while 33 (44.0%) undifferentiated (Figure 5, A-D). In nine Leukemia cases tumor differentiation was not done, as differentiation is not applicable.

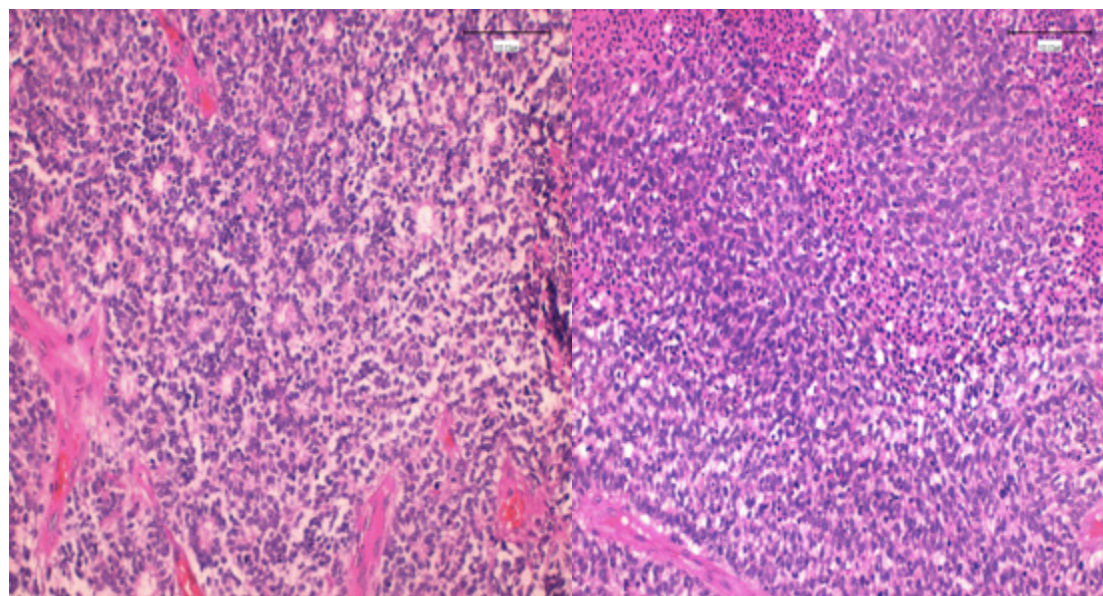


Figure 5: Well differentiated retinoblastoma from a 4 years old male, patient number 80 (A) Undifferentiated retinoblastoma from a 1 year old male, patient number 36 (B), Original Magnification X 200.

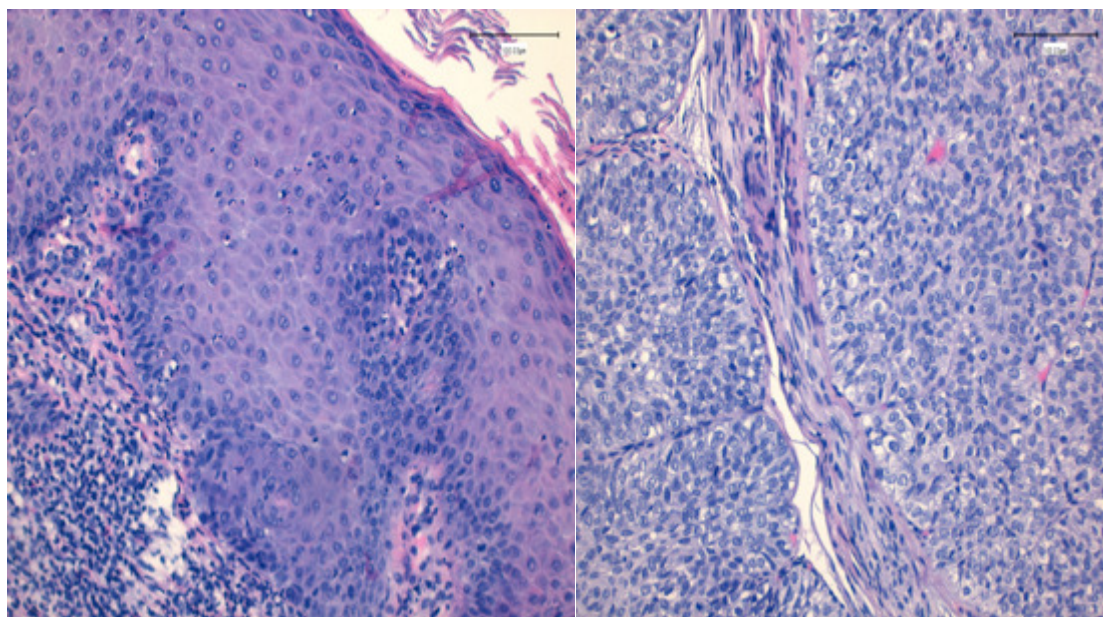


Figure 5: Well differentiated Squamous Cell Carcinoma from a 10 years old female, patient number 59 (C), Undifferentiated Squamous Cell Carcinoma from a 12 years old male, patient number 66 (D), Original Magnification X 200

Majority of Sarcoma 9 (69.2%), leukemia 6 (66.7%) and retinoblastoma 11 (52.4%) were undifferentiated tumors. Sarcoma was 2 times more likely to be undifferentiated as compared to retinoblastoma, $P = 0.48$ (Table 2).

Table 2: Distribution of tumor differentiation according to the type of pediatric malignancy (N=75)

Type of malignant tumor	Tumor differentiation		OR (95% CI)	*P-value
	Undifferentiated	Differentiated		
Retinoblastoma	11 (52.4%)	10 (47.6%)	1.0	
Squamous cell carcinoma	1 (7.7%)	12 (92.3%)	0.1 (0.0-0.7)	0.01
Sarcoma	9 (69.2%)	4 (30.8%)	2.0 (0.5-88)	0.48
Nephroblastoma	3 (30.0%)	7 (70.0%)	0.4 (0.1-1.9)	0.28
Lymphoma	4 (40.0%)	6 (60.0%)	0.6 (0.1-2.8)	0.70
Others	5 (62.5%)	3 (37.5%)	1.5 (0.3-8.0)	0.70

*Fisher's exact P-value, N (%)

Forty-one (97.6%) of the patients with well-differentiated malignant tumors survived within six months from the date the specimen was taken. Patients with undifferentiated pediatric malignancies were 13.1 times more likely to die within six months after specimen collection than with well differentiated (OR, 13.1; 95% CI, 1.5-111.2; $P < .009$), (Table 4).

Table 4: Histological differentiation vs. six-months survival rate (N=75)

Histological differentiation	Outcome at six months		OR (95% CI)	* <i>P</i> -value
	Died	Alive		
Undifferentiated	8 (24.2%)	25 (75.8%)		
Differentiated	1 (2.4%)	41 (97.6%)	13.1 (1.5-111.2)	0.009

*Fisher's exact *P*-value, N (%)

4. DISCUSSION

The retinoblastoma was the most malignant tumor followed by squamous cell carcinoma. The frequency of retinoblastoma was almost similar with the previous study by [7] at Ocean Road Cancer Institute in Tanzania. However, it differs with the study in Pakistan (38.9%) [10]. This may be due to the difference in social demographic and genetic susceptibility within Asia and Africa.

The current study has indicated that the Squamous cell carcinoma was the second most common malignant tumor among pediatric malignancies. A study by [7] in Tanzania showed very low frequency of Squamous cell carcinoma. Most of the patients with Squamous cell carcinoma in the current study were patients with Xeroderma pigmentosa and albinism who frequently attended dermatology clinic at KCMC where the Regional dermatology training centre is present with frequently outreach and special program which contribute to patient referral for surgery at the institution.

With regards to tumor differentiation, approximately more than half of the patients had well differentiated tumor. Majority of the undifferentiated malignant tumors were sarcoma and retinoblastoma. This may be attributed by facts that these tumors tend to have embryonic origin such as retinoblastoma or early childhood presentation within rapid growing cells, in others cases might have been diagnosed at late stages of the disease [11].

The overall six-months survival rate in this study was high. However, the results are incomparable to findings of a study in South Africa [9] where the survival rate was found to decrease with an increase in the duration of follow up. The higher survival rate observed in this current study was likely to be associated with short duration of follow up.

In our study, most of the patients with well-differentiated malignant tumors survived within six months from the date the specimens were taken. This means patients with undifferentiated malignancies were 13.1 times more likely to die within six months after specimens were taken than with well differentiated ones. This finding conforms to a common trend that well differentiated malignant tumors have higher survival rates as compared to undifferentiated ones [11].

Leukemia had the lowest survival rate due to lack of treatment protocol and medication in our set up which necessitate referrals to Muhimbili National hospital in Dar es Salaam where the treatment were offered. However, majority of participants were unable to access care due to financial or poor conditions and could not travel to Dar es Salaam, hence died at home without accessing proper treatment (this came up during phone follow up for survival data). Moreover, delays in seeking and receiving care for patients with malignancy as well as diagnosis challenges may play a major impact on initiation of treatment and hence low survival rate [12].

5. CONCLUSION

Retinoblastoma and squamous cell carcinoma are the most common pediatric malignant tumors among pediatric malignant tumors biopsied at Kilimanjaro Christian Medical Centre. The overall six-months survival rate is high when early detection of childhood malignancies is practicable.

ETHICAL APPROVAL

The ethical approval was sought and obtained from Kilimanjaro Christian Medical University College Research and Ethics Committee, with the Certificate number 920. The permission to conduct the study at KCMC was sought from the Department of Anatomy and Neuroscience, Department of Pathology and Department of Dermatology. Confidentiality was maintained throughout the research period.

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